Frühlingszyklus 17.03.2022, LUKS

Radiotherapie bei ZNS Metastasen

Prof Dr Gabriela Studer
CAe Radio-Onkologie LUKS

HISTORIE

wait till symptoms
→ CT (MRI)
→ **WBRT**

wait till symptoms
→ CT (MRI)
→ **WBRT** (SRT/SRS)

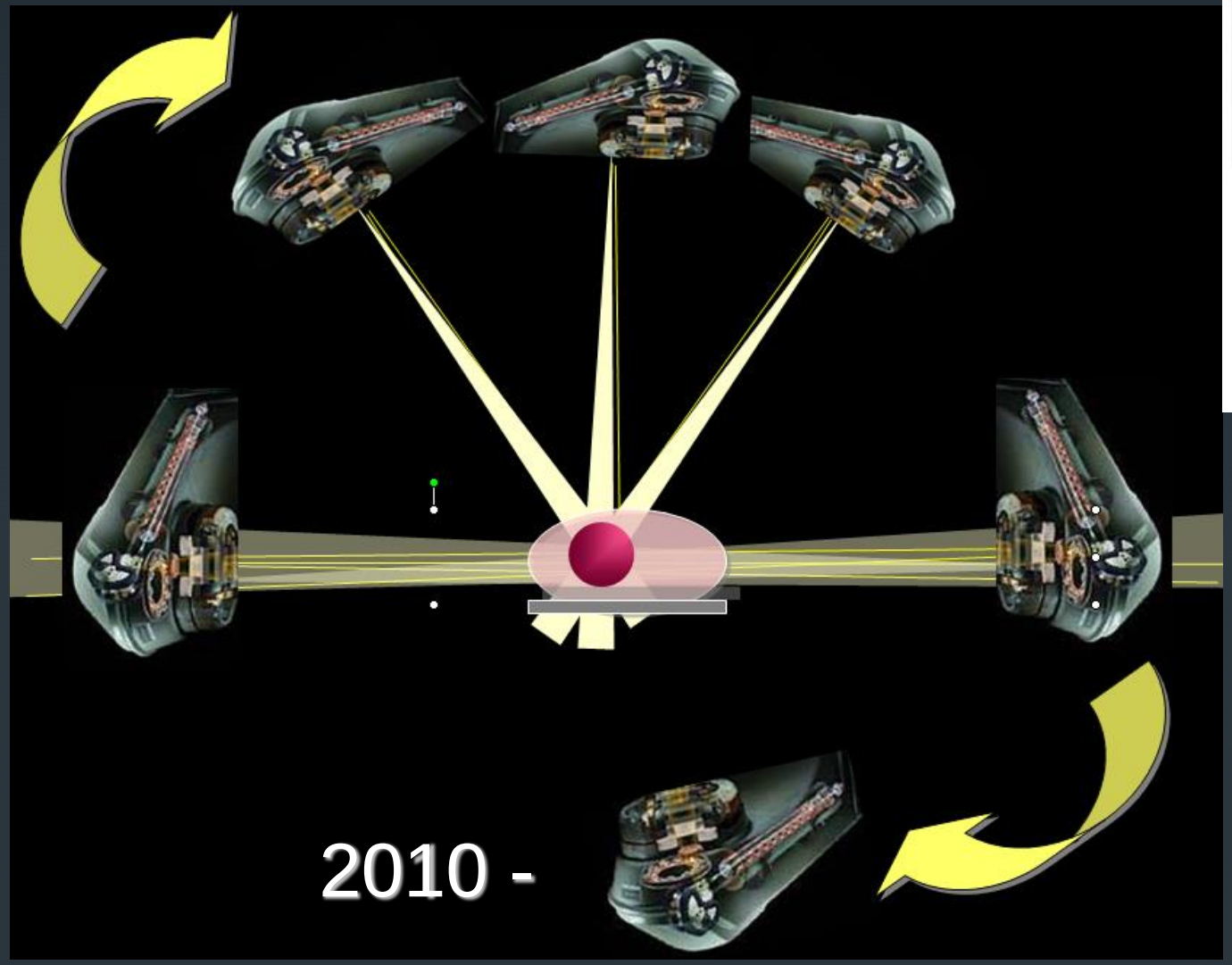
search for lesions:
→MRI (CT) CNS FU:
WBRT +/or SRT/SRS

search for lesions:
→ MRI (CT) CNS FU:
→ **SRT/SRS** or **WBRT +/- HA**

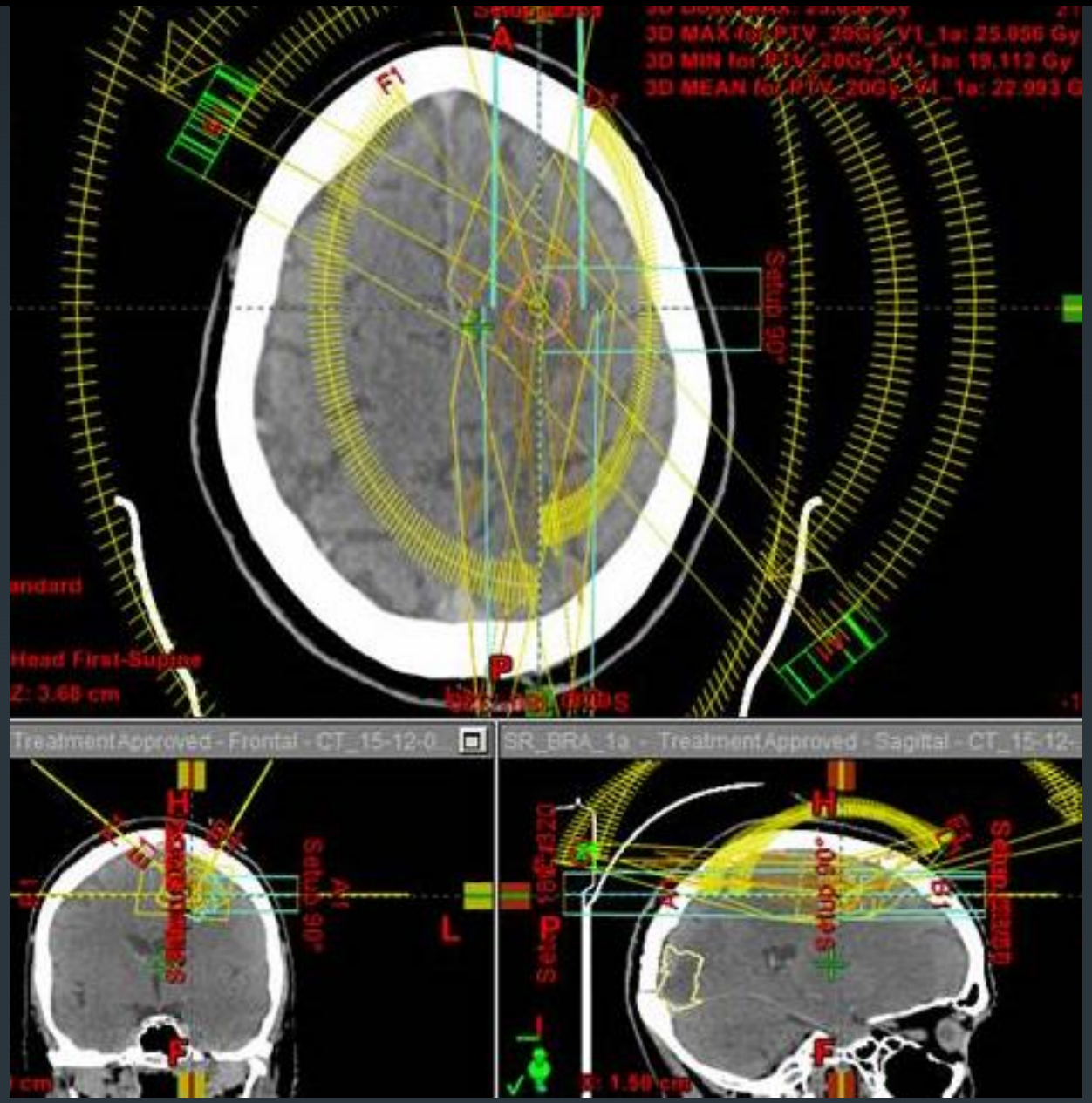
small / multiple lesions:…
? wait ? new CNS effective drug?

1990 2000 2010 2020 2022

VMAT



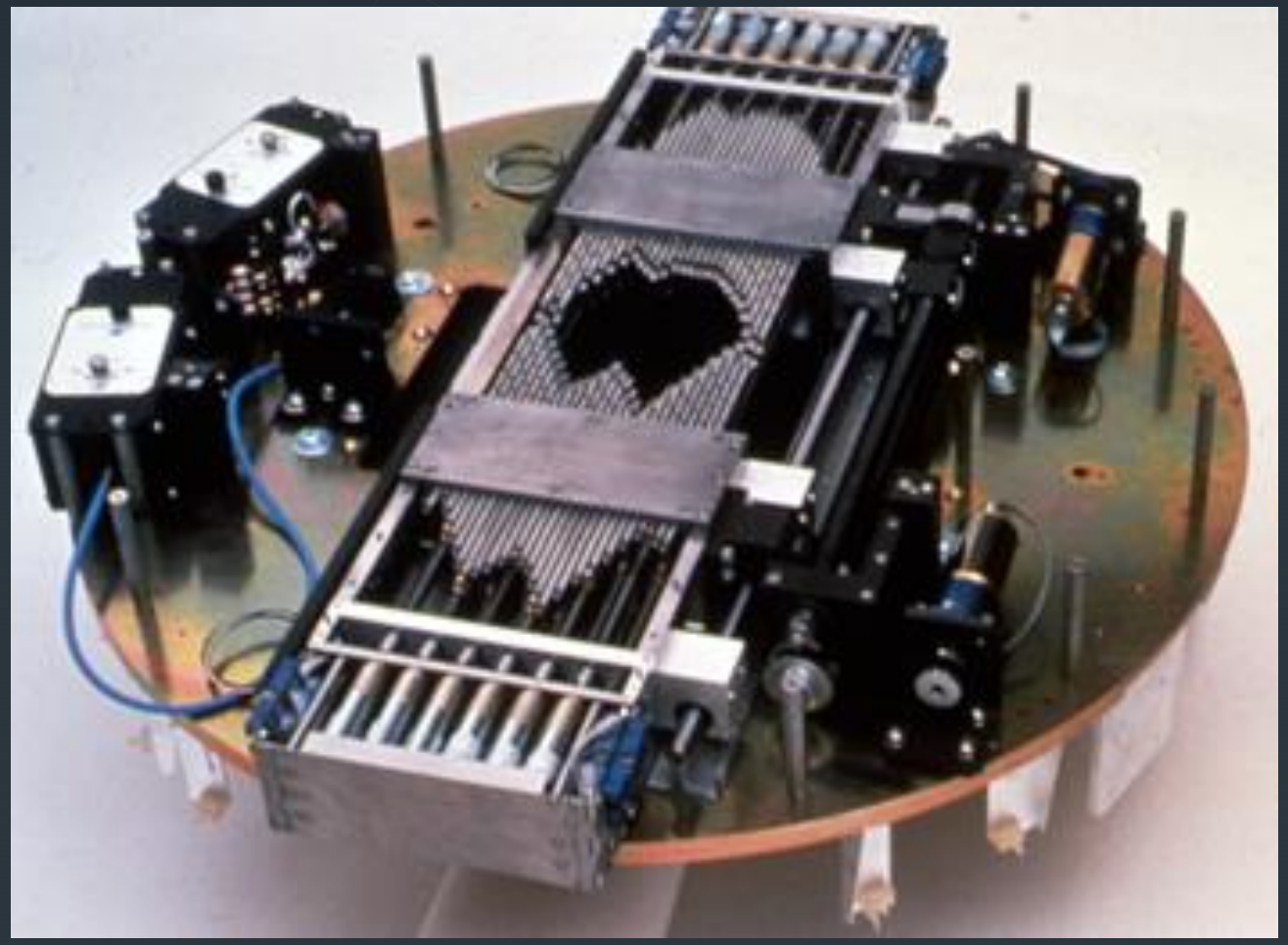
VMAT

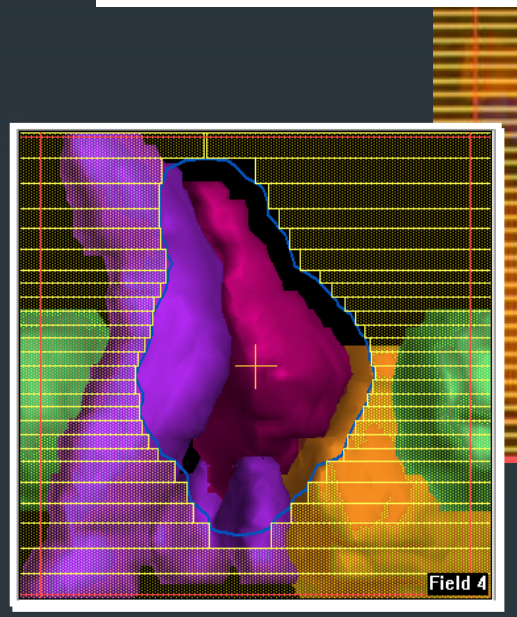

Treatment Approved - Frontal - CT_15-12-0
SR_BRA_1a - Treatment Approved - Sagittal - CT_15-12-

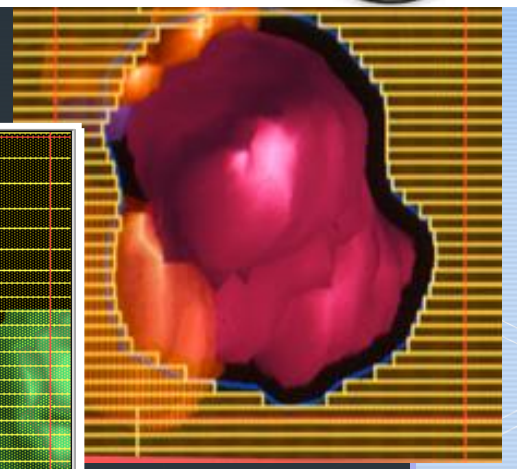

VARIAN
iX BEAM

VMAT

IMRT: Multi Leaf Collimators







Therapeutische Prinzipien

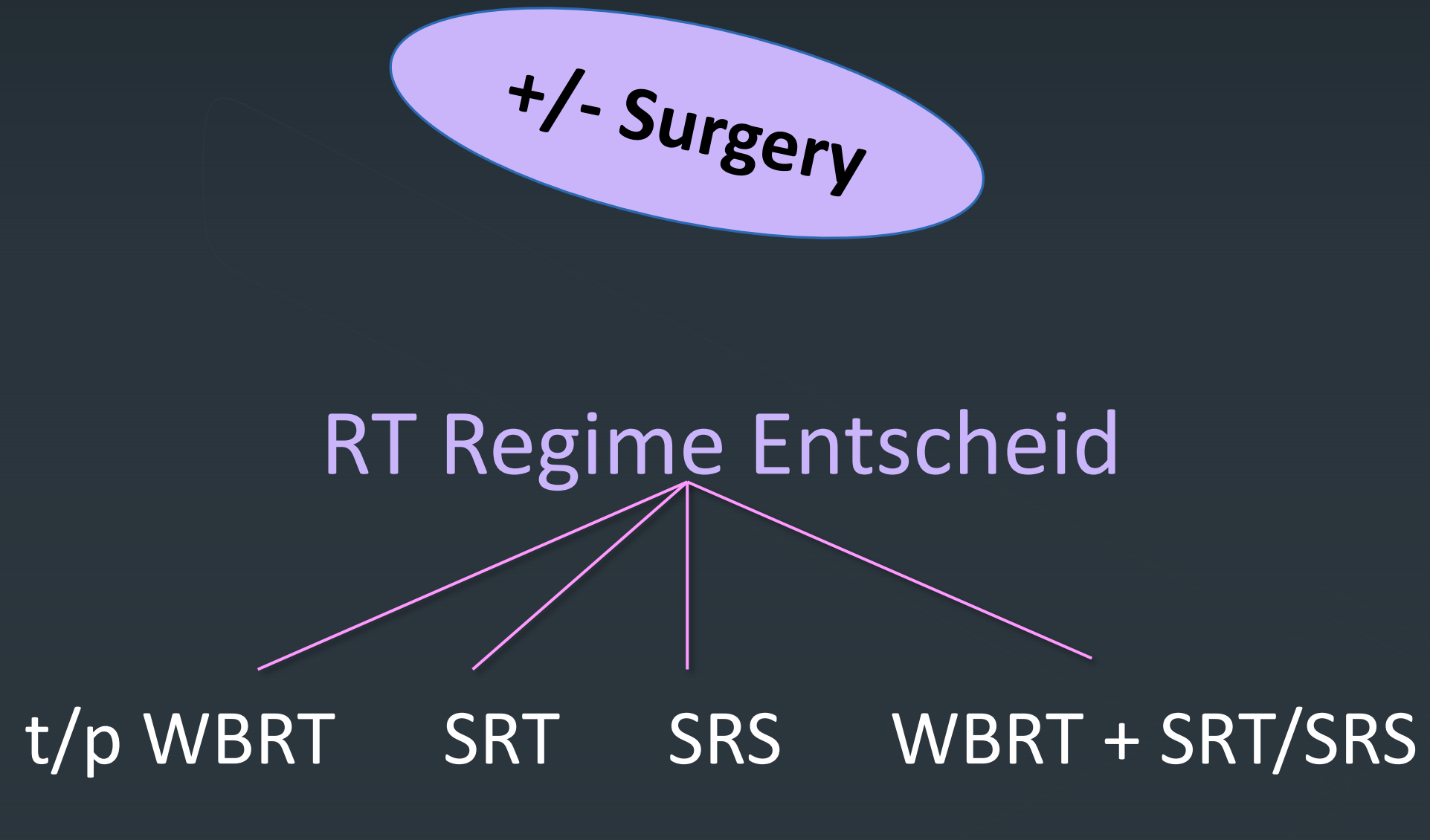
1) TUB Empfehlung:

- RT-Indikation ?
- Tx-Sequenz bei Multimodalität ?

2) radio-onkologische Entscheidung:

- RT-Volumen ?
- RT-Technik ?
- RT-Regime ?

Therapeutische Prinzipien



peutische Prinzipien

VOLUME 32 · NUMBER 34 · DECEMBER 1 2014

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Preservation of Memory With Conformal Avoidance of the Hippocampal Neural Stem-Cell Compartment During Whole-Brain Radiotherapy for Brain Metastases (RTOG 0933): A Phase II Multi-Institutional Trial

Vinai Gondi, Stephanie L. Pugh, Wolfgang A. Tome, Chip Caine, Ben Corn, Andrew Kanner, Howard Rowley,

RT Regime Entscheid

t/p WBRT SRT SRS WBRT + SRT/SRS

VOLUME 32 · NUMBER 34 · DECEMBER 1 2014

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

peutische Prinzipien

Conclusion

Conformal avoidance of the hippocampus during WBRT is associated with preservation of memory and QOL as compared with historical series.

RT Regime Entscheid

t/p WBRT SRT SRS WBRT + SRT/SRS

Hippocampal Avoidance During Whole-Brain Radiotherapy Plus Memantine for Patients With Brain Metastases: Phase III Trial NRG Oncology CCO01

Paul D. Brown, MD[1]; Vinai Gondi, MD[2]; Stephanie Pugh, PhD[3]; Wolfgang A. Tome, PhD[4]; Jeffrey S. Wefel, PhD[5]; Terri S. Armstrong, PhD[6]; Joseph A. Bovi, MD[7]; Cliff Robinson, MD[8]; Andre Konski, MD, MBA[9]; Deepak Khuntia, MD[10]; David Grosshans, MD, PhD[5]; Tammie L. S. Benzinger, MD, PhD[8]; Deborah Bruner, PhD[11]; Mark R. Gilbert, MD[6]; David Roberge, MD[12]; Vijayananda Kundapur, MD[13]; Kiran Devisetty, MD[14]; Sunjay Shah, MD[15]; Kenneth Usuki, MD[16]; Bethany Marie Anderson, MD[17]; Baldassarre Stea, MD, PhD[18]; Harold Yoon, MD[19]; Jing Li, MD[5]; Nadia N. Laack, MD[1]; Tim J. Kruser, MD[20]; Steven J. Chmura, MD, PhD[21]; Wenyin Shi, MD[22]; Snehal Deshmukh, MS[3]; Minesh P. Mehta, MD[23]; and Lisa A. Kachnic, MD[24] for NRG Oncology

J Clin Oncol 38. © 2020 by American Society of Clinical Oncology

erapeutische Prinzipien

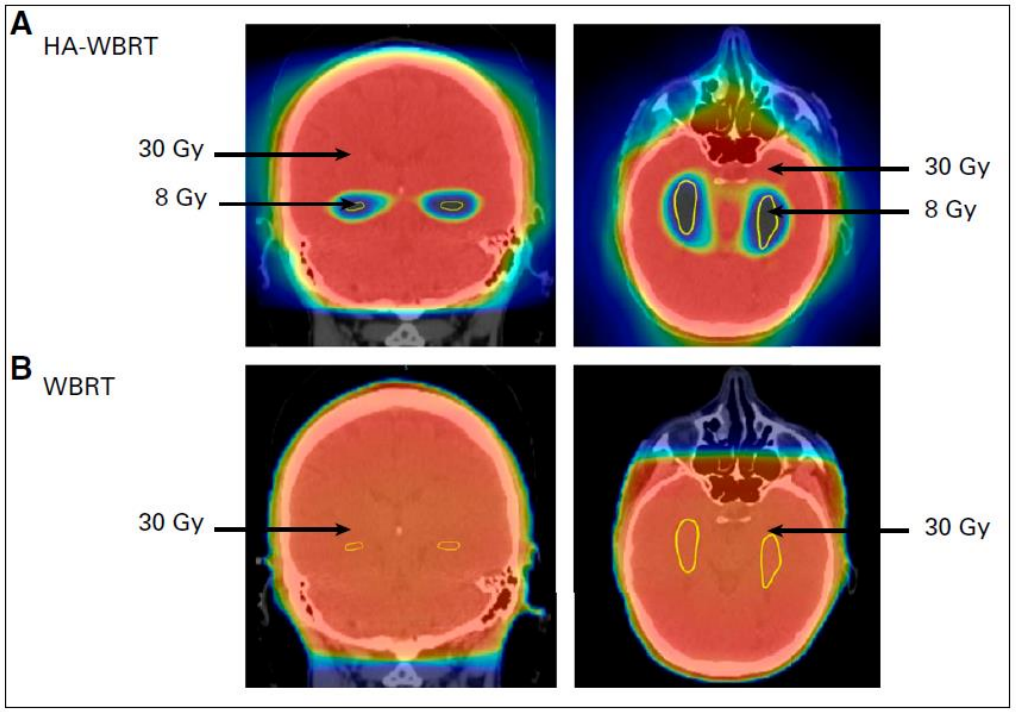


FIG 1. Several-fold reduction in radiation dose to hippocampi (yellow) using (A) hippocampal avoidant whole-brain radiotherapy (HA-WBRT) *v* (B) conventional WBRT.

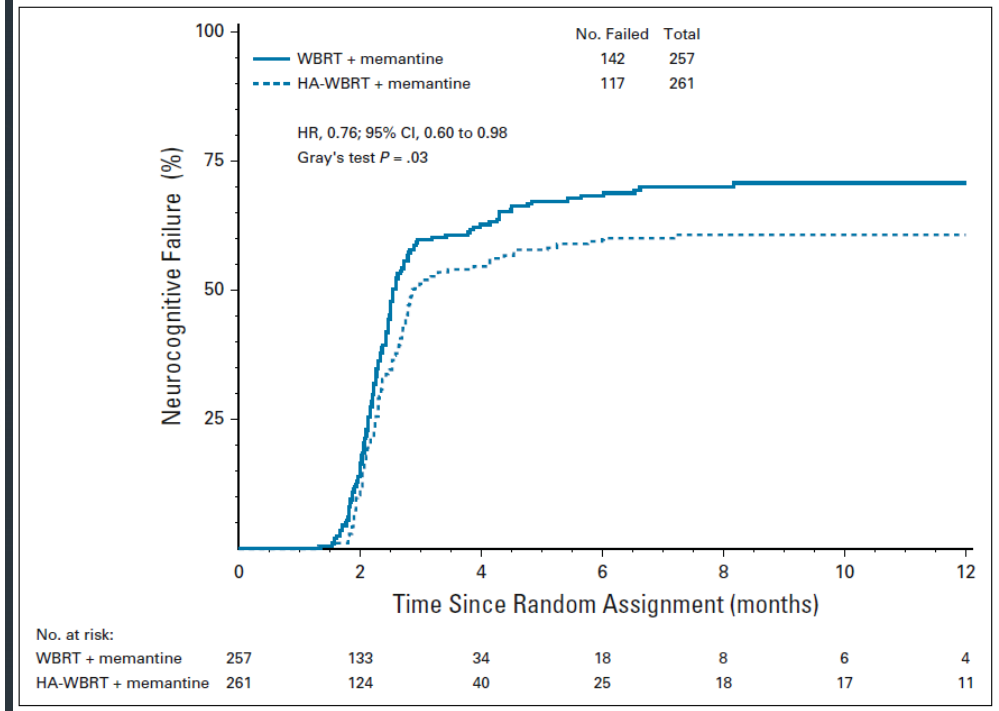


FIG 3. Kaplan-Meier graph showing time to cognitive failure. HA, hippocampal avoidance; WBRT, whole-brain radiotherapy.

International Journal of Radiation Oncology*Biology*Physics
Volume 91, Issue 4, 15 Marc 2015 Pages 781-786

Therapeutische Prinzipien

RISK for 'protecting' hippocampal area ??

Risk of Hippocampal Metastases in Small Cell Lung Cancer Patients at Presentation and After Cranial Irradiation: A Safety Profile Study for Hippocampal Sparing During Prophylactic or Therapeutic Cranial Irradiation

Vijayananda Kundapur, MD, DMRT, FRCR,* Tasha Ellchuk, FRCPC,‡ Shahid Ahmed, FRCPC,* and Vinai Gondi, MD§

Results: Seventy eligible patients were identified. Of 59 patients presenting with de novo BM, 3 patients (5%, 95% confidence interval [CI]: 0%-10.7%) had HM. Collectively there were 359 (range, 1-33) de novo BM with 3 (0.8%, 95% CI: 0%-1.7%) HM deposits. Twenty patients experienced progression of metastatic disease in the brain after WBRT. Of the 20 patients, only 1 patient (5%, 95% CI: 0%-14.5%) experienced HM. On logistic regression, no factors significantly correlated with HM.

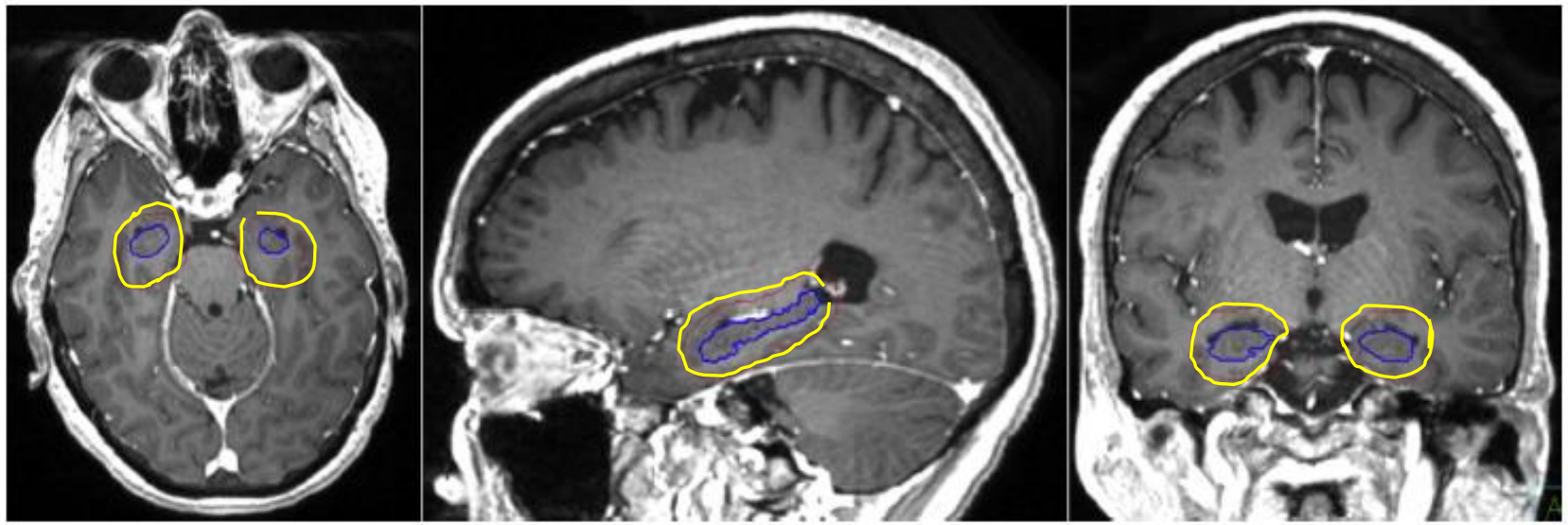
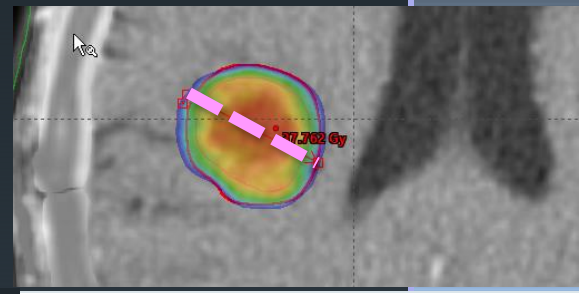
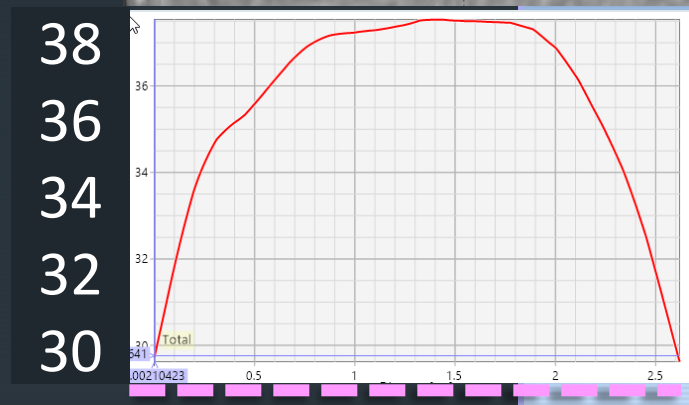


Fig. 1. Contrast enhanced T1 magnetic resonance images showing the hippocampus (HC) contoured in blue and the hippocampal avoidance (HA) region contoured in red. The region of the brain outside the HA region is the rest of the brain. A color version of this figure is available at www.redjournal.org

Therapeutische Prinzipien

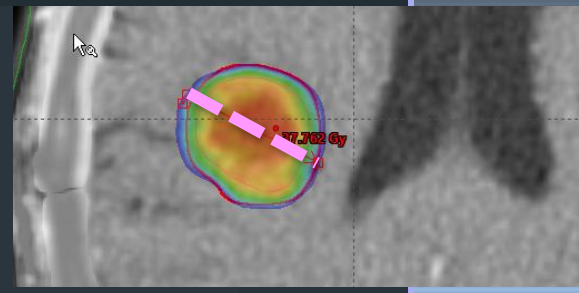




RT Regime Entscheid

WBRT **SRT** **SRS** WBRT + SRT/SRS

Therapeutische Prinzipien



SRS/SRT: kleinere Herde, 1-~6 Läsionen

SRS: 1 Fraktion

SRT: 5-6 Fraktionen

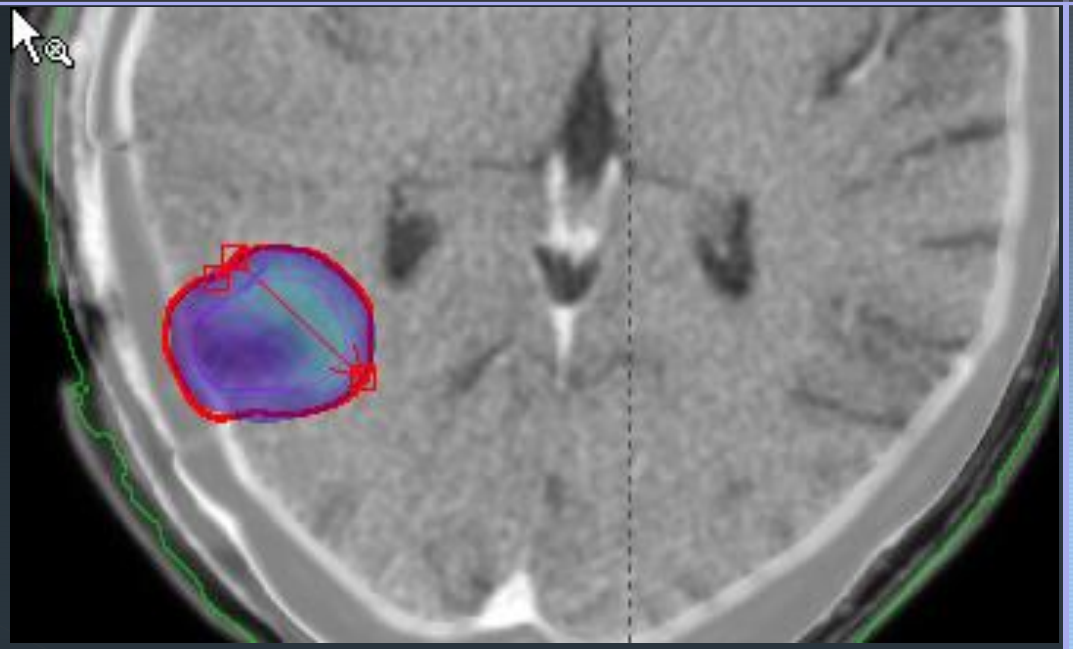
WBRT: viele Herde, kurzer Zeithorizont, schlechter PS

→ +/- Hippocampus-Schonung

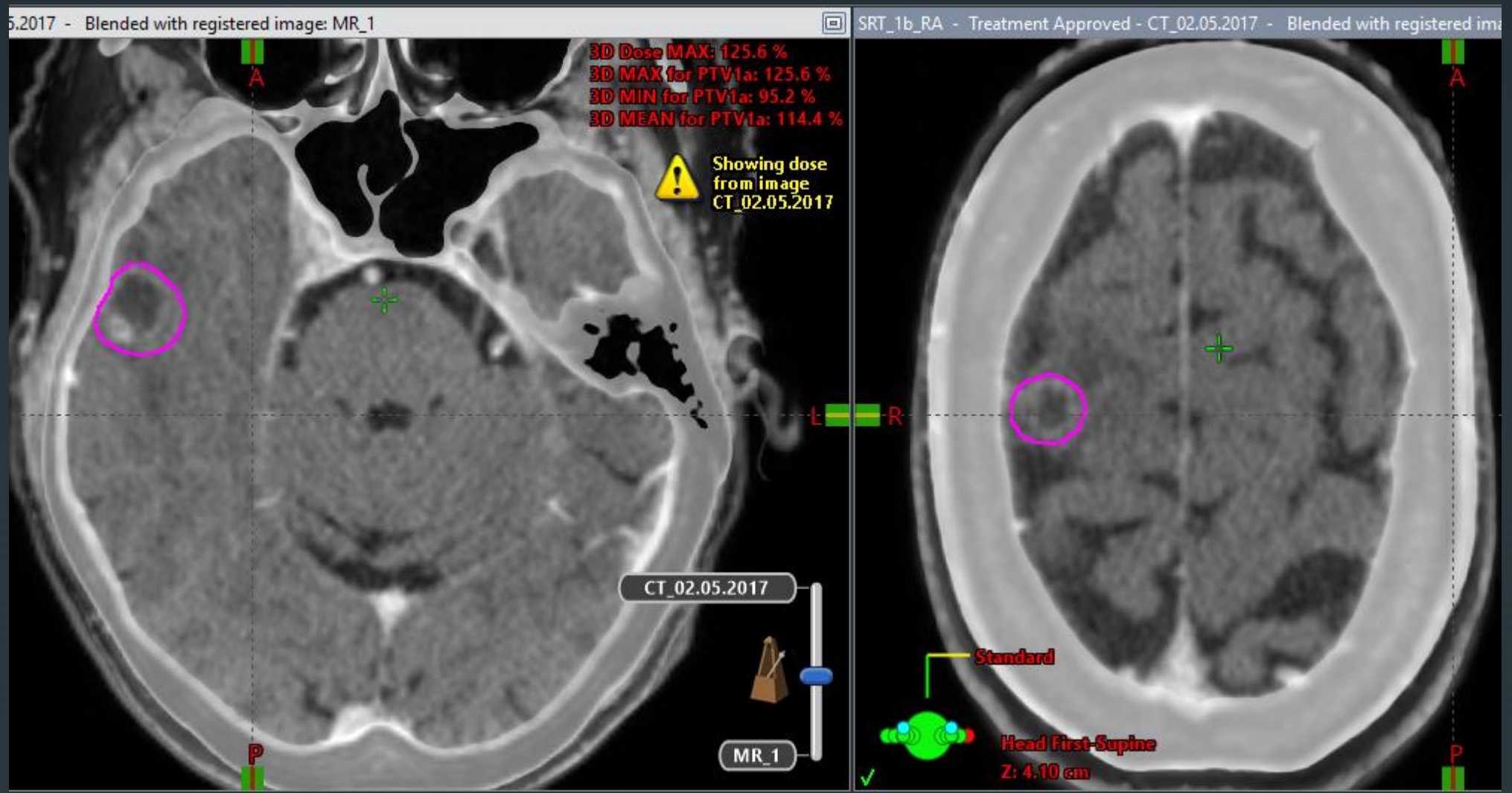
→ +/- SRT boost

Therapeutische Prinzipien

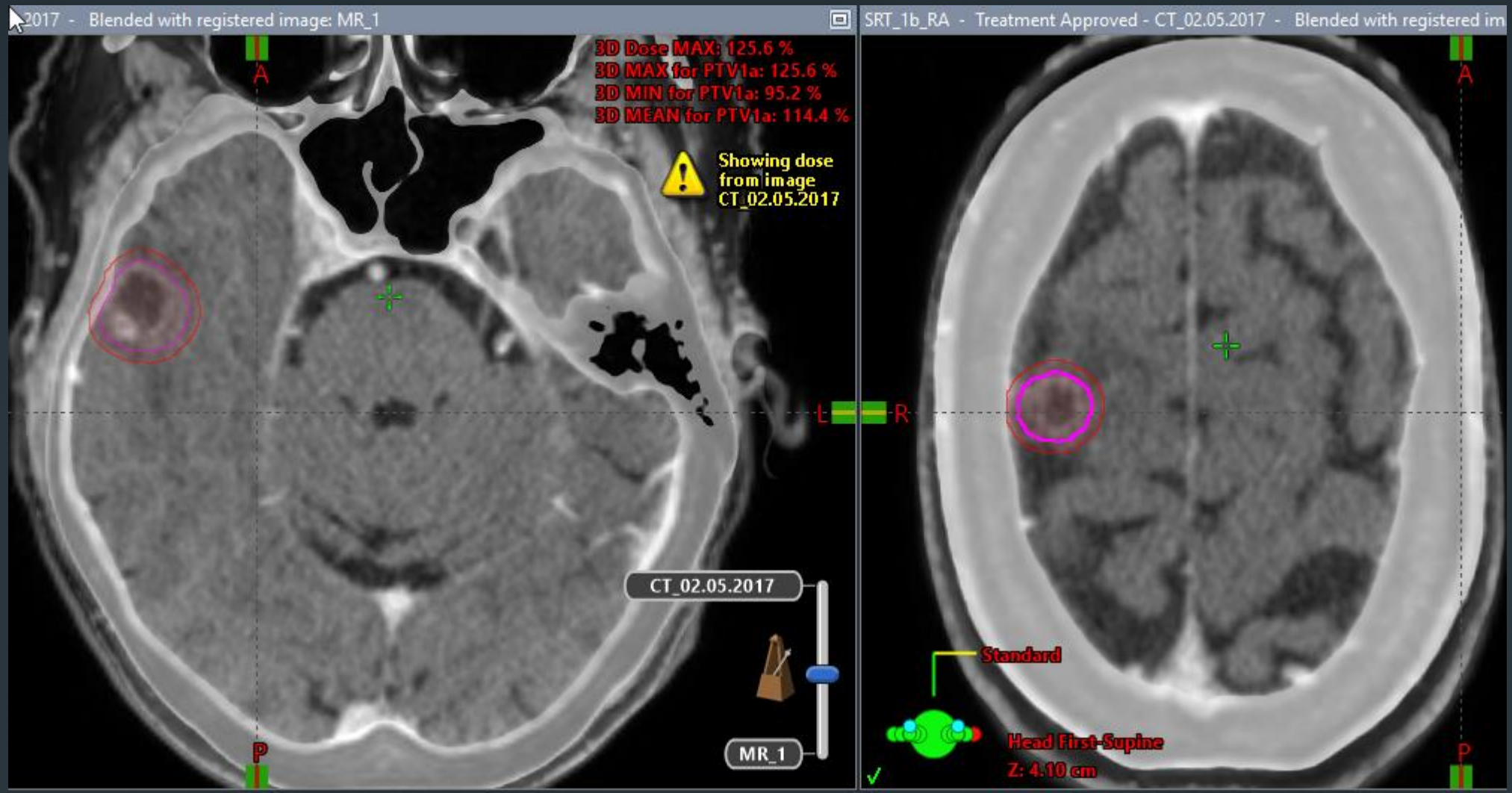
postop. SRT
(kleinere Herde)



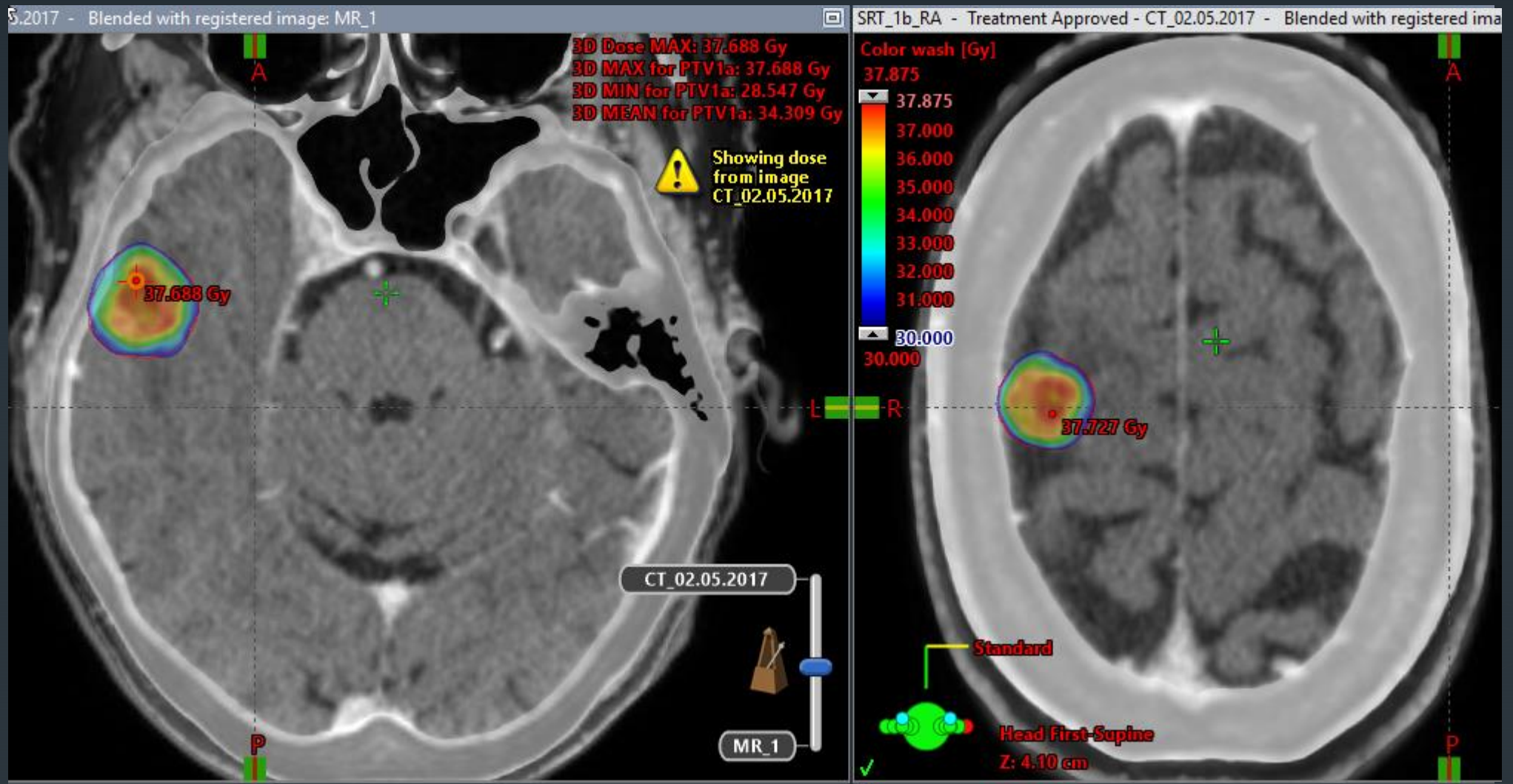
GTV


5.2017 - Blended with registered image: MR_1
3D Dose MAX: 125.6 %
3D MAX for PTV1a: 125.6 %
3D MIN for PTV1a: 95.2 %
3D MEAN for PTV1a: 114.4 %
Showing dose from image CT_02.05.2017
A
L
P
CT_02.05.2017
MR_1
SRT_1b_RA - Treatment Approved - CT_02.05.2017 - Blended with registered ima
A
R
P
Standard
Head First-Supine
Z: 4.10 cm

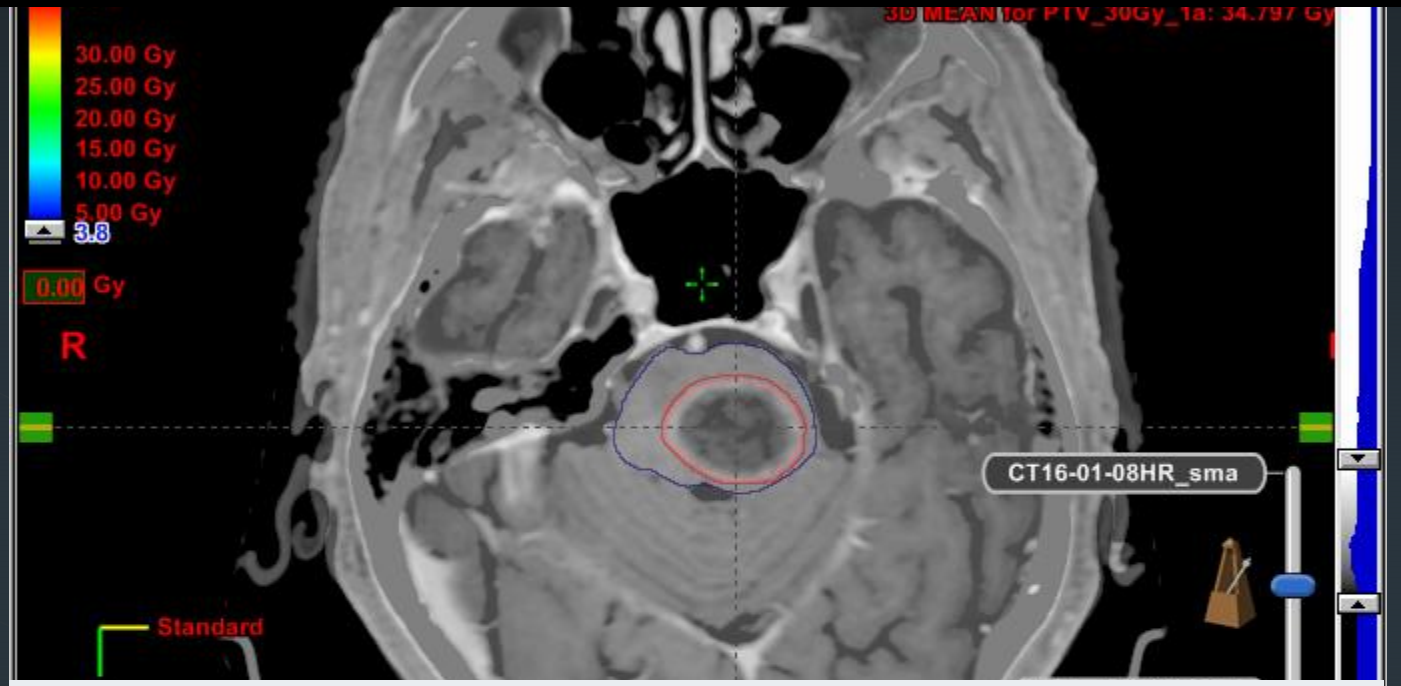
0-2 mm margin PTV



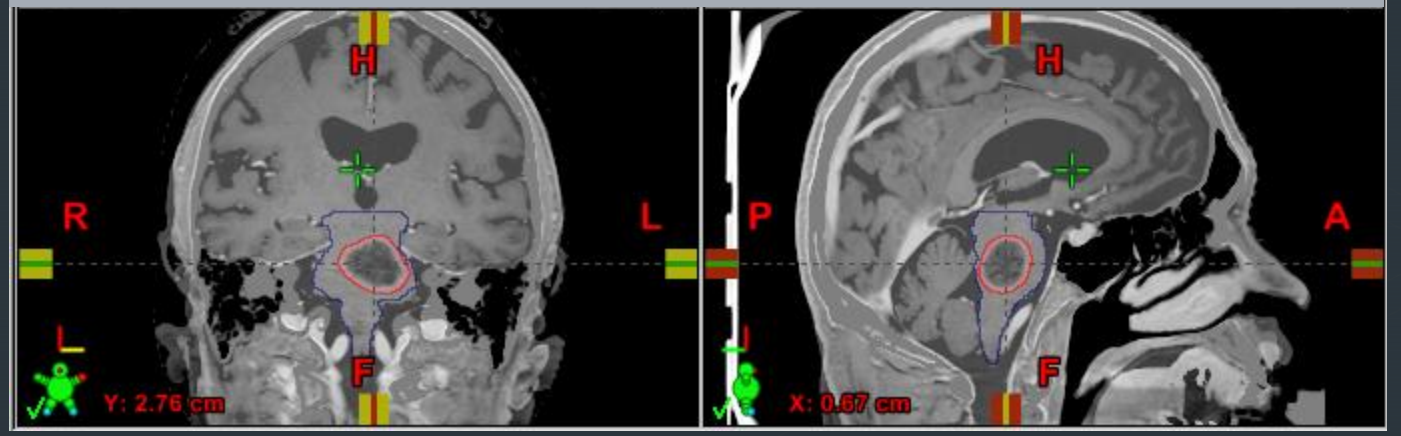
6x 5Gy @ 80%


5.2017 - Blended with registered image: MR_1
3D Dose MAX: 37.688 Gy
3D MAX for PTV1a: 37.688 Gy
3D MIN for PTV1a: 28.547 Gy
3D MEAN for PTV1a: 34.309 Gy
Showing dose from image CT_02.05.2017
37.688 Gy
A
P
L
R
CT_02.05.2017
MR_1
SRT_1b_RA - Treatment Approved - CT_02.05.2017 - Blended with registered ima
Color wash [Gy]
37.875
37.875
37.000
36.000
35.000
34.000
33.000
32.000
31.000
30.000
30.000
37.727 Gy
Standard
Head First-Supine
Z: 4.10 cm

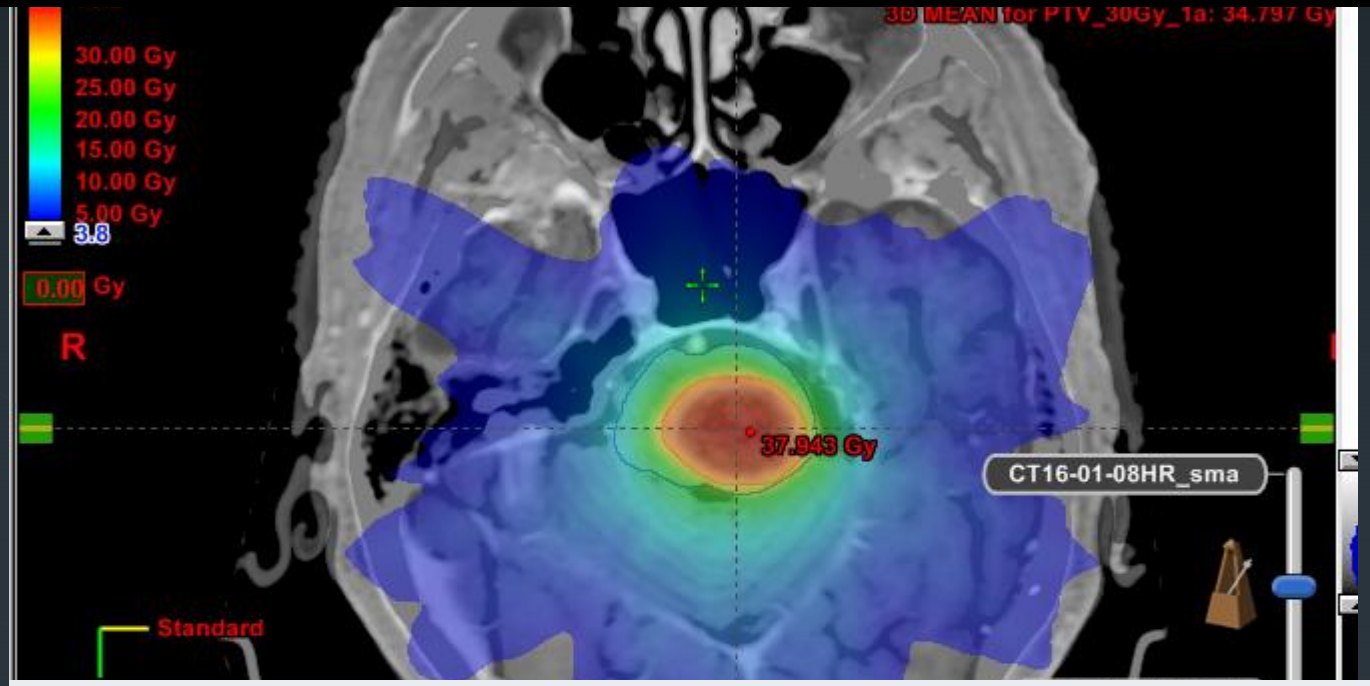
SRS/SRT



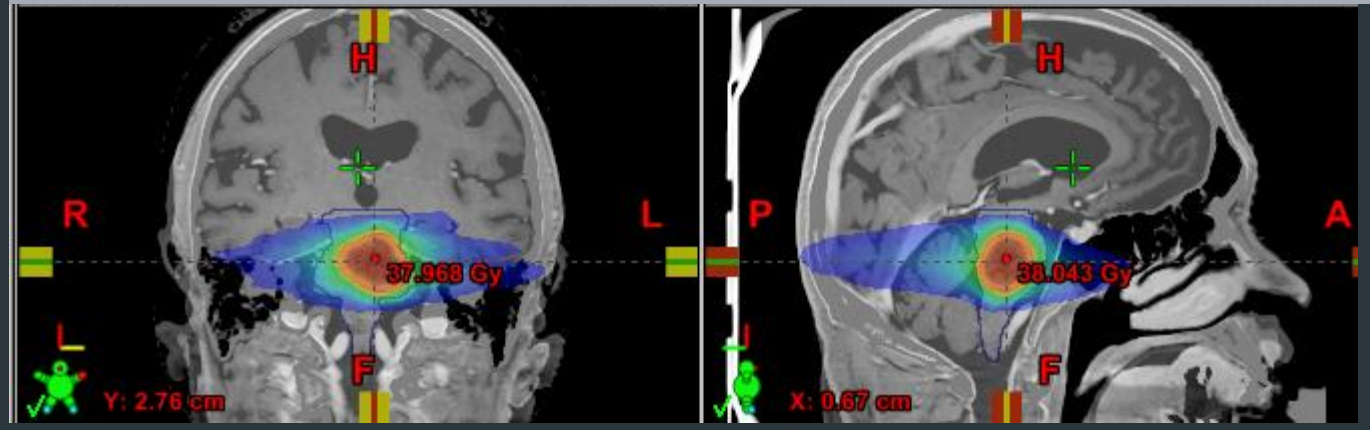
brain stem M 6x5Gy @80% & PDN



SRS/SRT

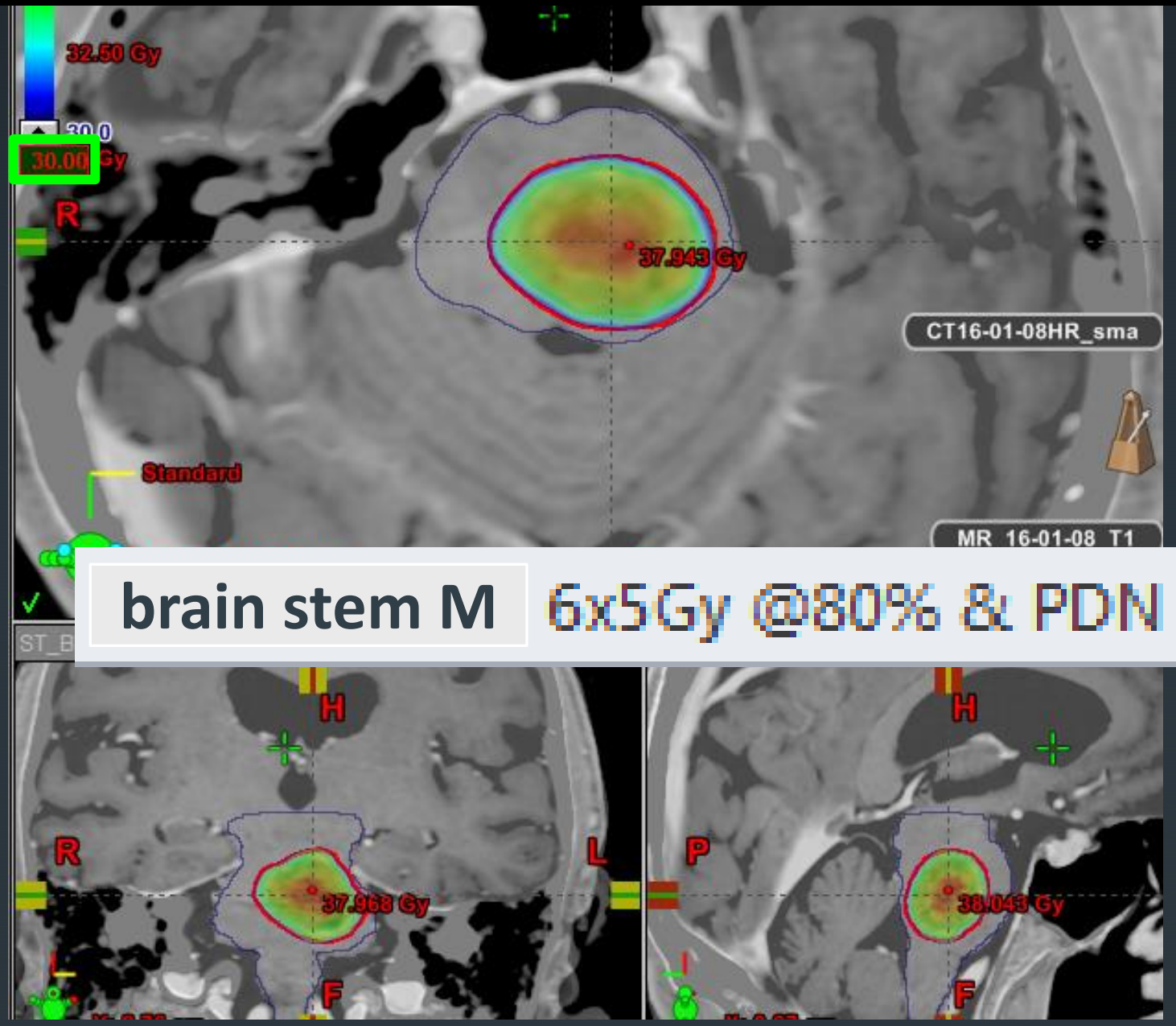


brain stem M 6x5Gy @80% & PDN



hoch präzise / hoch konformal

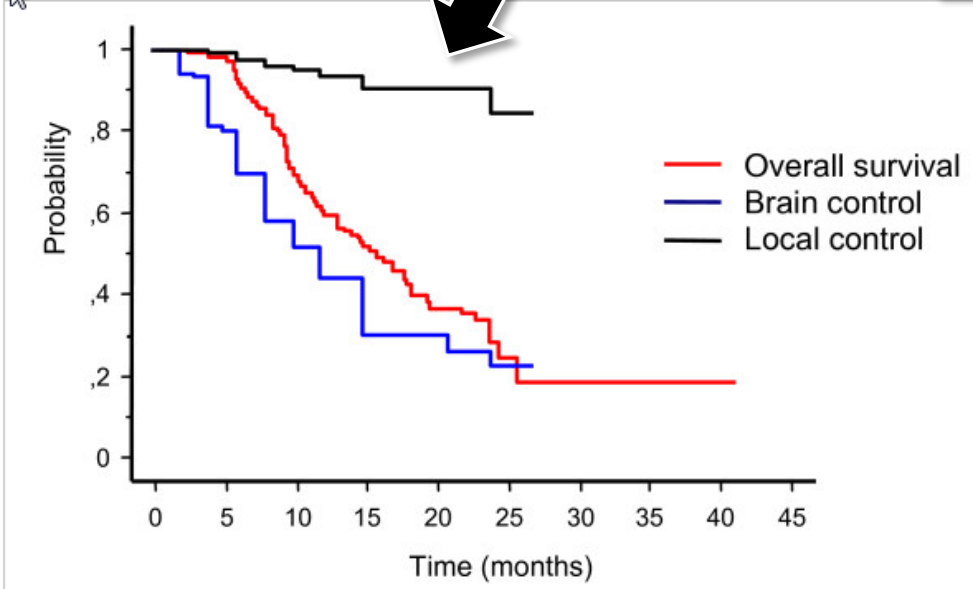
SRS/SRT



Lokalkontrolle nach SRS/SRT

Radiat Oncol. 2011; 6: 48.

Figure 1



Kaplan-Meier analysis of overall survival, brain control, and local control

TOLERANZ SRS/SRT

Früheffekte:

- eventuell fokale Alopezie
- ((passager Kopfschmerzen))
- (etwas Müdigkeit)

TOLERANZ SRS/SRT

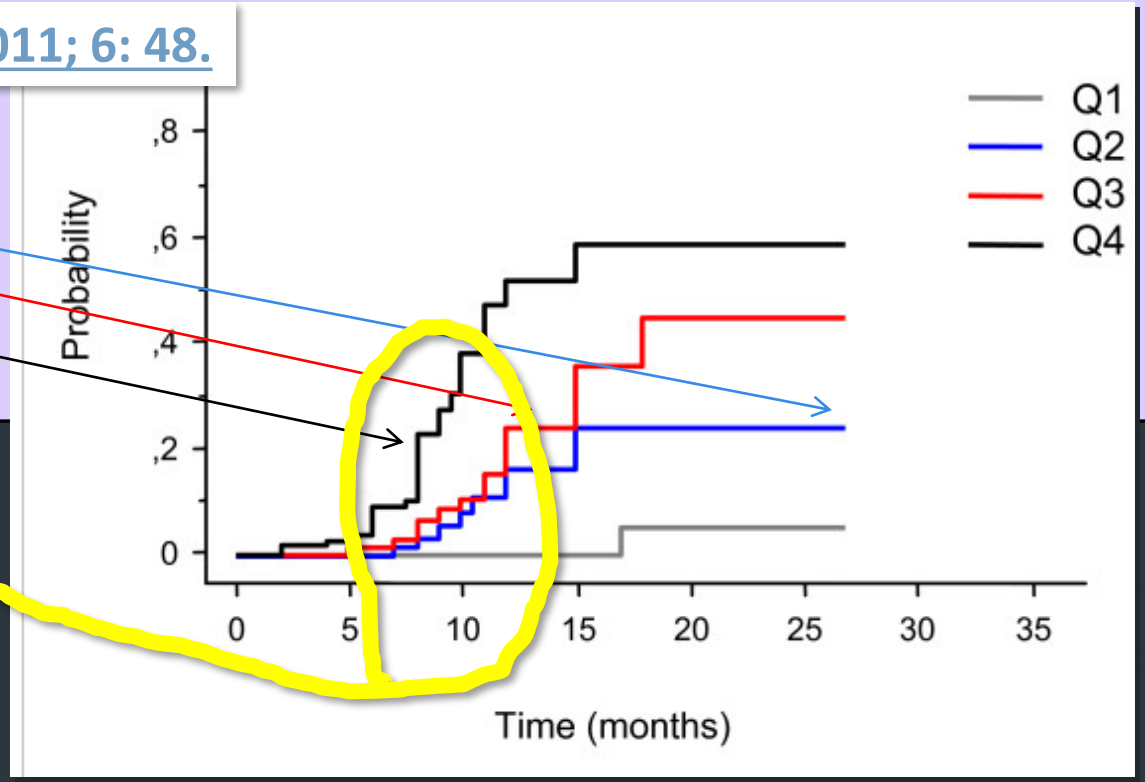
Späteffekte:

risk of brain radionecrosis after SRS for brain M in relation **to brain volumes receiving 12 Gy** (V12 Gy) stratified for quartiles (Q1-Q4).

Q1 < 3.3 cm³,
Q2 3.3-5.9 cm³,
Q3 6.0-10.9 cm³,
Q4 >10.9 cm³

actuarial risk at 1 year:
0% for Q1,
16% for Q2,
24% for Q3,
51% for Q4

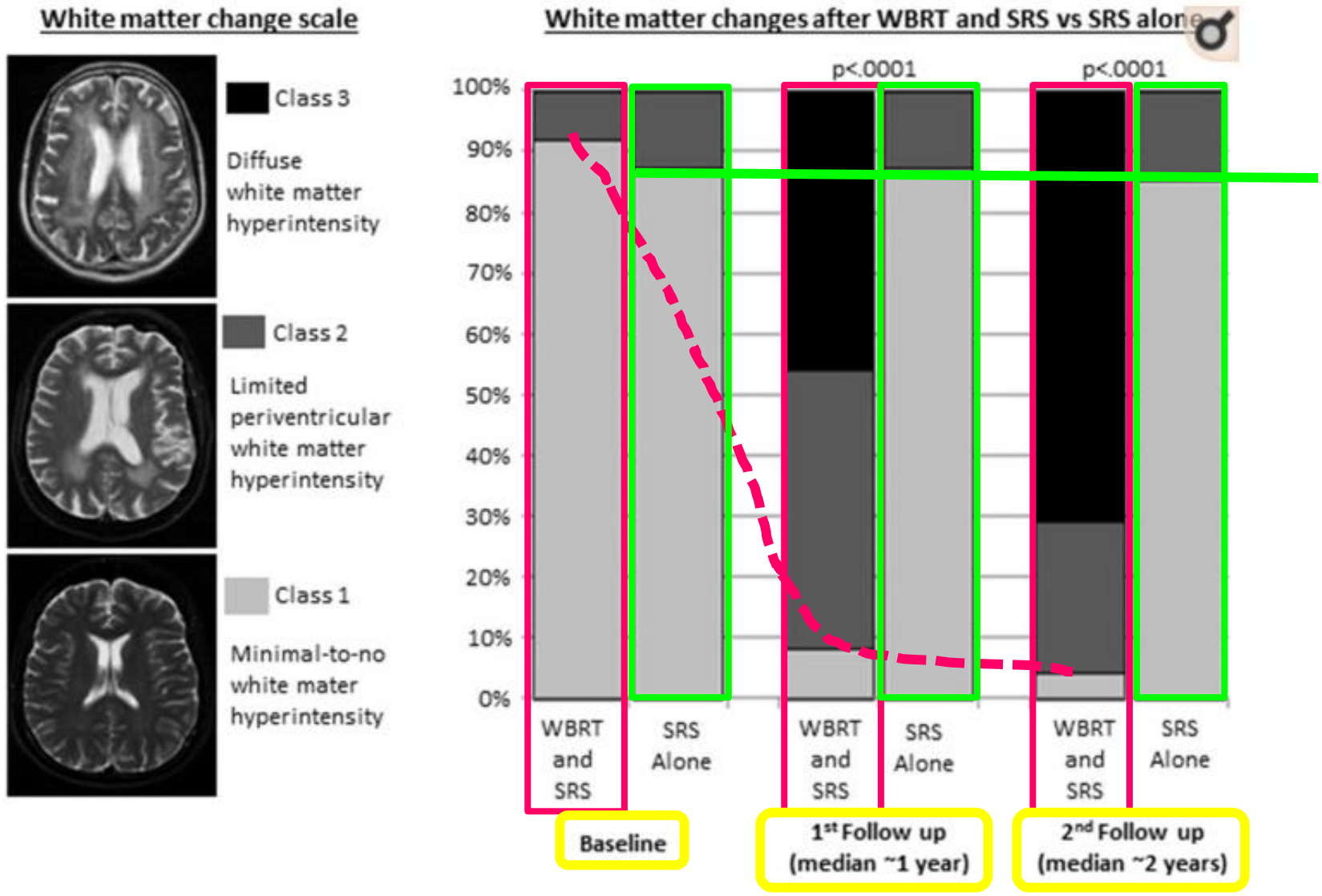
Radiat Oncol. 2011; 6: 48.



frontiers in Oncology

published: 09 Oct[illegible]er 2018
doi: 10.3389/fonc.20[illegible]

Figure 1



White matter changes in patients with non-small cell lung cancer brain metastases treated with whole brain radiation therapy (WBRT) and stereotactic radiosurgery (SRS) ($n = 37$) or SRS alone ($n = 31$). Adapted from Monaco et al. (39) with permission from the publisher.

frontiers in Oncology

published: 09 Oct[illegible]er 2018
doi: 10.3389/fonc.201[illegible]

Strategies to Preserve Cognition in Patients With Brain Metastases: A Review

*Tyler P. Robin and Chad G. Rusthoven**

Department of Radiation Oncology, University of Colorado School of Medicine, Aurora, CO, United States

increasing number of CNS effective drugs;

no standards yet

TABLE 1 | Selected studies supporting CNS efficacy for systemic agents in melanoma, lung, and breast cancer.

References	Eligibility	No. of pts	Drug	Methods	Outcomes
Margolin et al. (9)	Metastatic melanoma with BM (divided into cohorts for symptomatic or asymptomatic)	72	Ipi	Phase II	CNS disease control: 24% in asymptomatic cohort 10% in symptomatic cohort
Goldberg et al. (13)	Untreated asymptomatic BM from melanoma or NSCLC	36	Pembro	Phase II	CNS response: melanoma: 22% NSCLC: 33%
Long et al. (19)	Untreated asymptomatic melanoma BM with no previous local brain therapy	79	Nivo OR Ipi/Nivo	Randomized Phase II	CNS response: Ipi/Nivo: 46% Nivo: 20% Nivo (after failed local therapy, symptomatic, or with LMD): 6%
Davies et al. (14)	Metastatic melanoma with BM cohorts: (A)$BRAF^{V600E}$/asymptomatic/no prior local brain therapy/ECOG 0/1 (B) $BRAF^{V600E}$/asymptomatic/prior local brain therapy/ECOG 0/1 (C) $BRAF^{V600D/K/R}$/asymptomatic/ with or without prior local brain therapy/ECOG 0/1 (D) $BRAF^{V600D/E/K/R}$/symptomatic/ with or without prior local brain therapy/ECOG 0/1/2	125	D/T	Phase II	CNS response: (A) 58% (B) 56% (C) 44% (D) 59% Duration of response (median): (A) 6.5 months (B) 7.3 months (C) 8.3 months (D) 4.5 months
Gadgeel et al. (12)	ALK-positive NSCLC after prior crizotinib (Pts with measurable CNS disease were pooled from two single-arm phase II studies)	50 pts with measurable CNS lesions	Alectinib	Pooled analysis of 2 Phase II studies	CNS response: 64.0% Duration of response (median): 10.8 mo
Peters et al. (17)	Previously untreated advanced ALK-positive NSCLC	Total: 303 BM: 43 pts with measurable CNS lesions	Crizotinib OR alectinib	Phase III	CNS response: crizotinib: 50% alectinib: 81% Duration of response (median): crizotinib: 5.5 months alectinib: 17.3 months
Goss et al. (15)	T790M-positive advanced NSCLC after progression on other EGFR-TKI with >1 measurable CNS lesion (pooled analysis of two phase II trials)	50	Osi	Pooled analysis of 2 Phase II studies	CNS response: 54.0% Duration of response (median): NR Est duration of response: 75% at 9 mo
Wu et al. (20)	T790M-positive advanced NSCLC after progression on other EGFR-TKI. Planned subgroup analysis of AURA3 for patients with baseline CNS lesions.	46 pts with measurable CNS lesions	Osi	Planned subgroup analysis of phase III	CNS response: osimertinib: 70% Platinum-pemetrexed: 31%
Camidge et al. (18)	ALK-positive NSCLC (Exploratory analysis of pts with baseline brain metastases from two prospective studies): (1) phase I/II (NCT01449461) (2) phase II ATLA (NCT02094573) arm A (3) phase II ATLA (NCT02094573) arm B	Measurable (>10 mm) (1) 15 (2) 26 (3) 18	brigatinib	Exploratory analysis of a phase I/II and subsequent phase II study	CNS response (among pts with measurable (>10 mm) brain metastases: (1) 53% (2) 46% (3) 67%
Lin et al. (8)	HER2+ breast cancer after prior trastuzumab and progressive BM after prior WBRT or SRS	242	L	Phase II	CNS response: 6% (20% in patients on capecitabine-lapatinib expansion)
Bachelot et al. (10)	HER2+ breast cancer with BM not previously treated with WBRT, capecitabine, or lapatinib	45	X/L	Phase II	CNS response: 65.9%
Krop et al. (11)	Her2+ breast cancer after prior trastuzumab and a taxane (exploratory analysis of EMILIA limited to patients with pre-existing BM)	95	TDM-1 OR X/L	Exploratory analysis of Phase III study	CNS progression: TDM-1: 22.2%; XL: 16.0% Median overall survival: TDM-1: 26.8 mo; XL: 12.9 mo

BM, brain metastases; L, lapatinib; X, capecitabine; X/L, capecitabine and lapatinib; TDM-1, trastuzumab emtansine; Ipi, ipilimumab; Pembro, pembrolizumab; Nivo, nivolumab; LMD, leptomeningeal disease; D, abrafenib; T, tramatinib; Osi, osimertinib; pem, pemetrexed; platinum, cisplatin or carboplatin; NR, not reached.

TAKE HOME

ZNS-M RT-Indikation

1. interdisziplinär: Indikation?/Sequenz?

2. gelegentlich zuwarten mit RT, so neue Substanzen verfüglich

TAKE HOME

ZNS-M RT

1. heute meist SRS/SRT statt WBRT
2. SRS/SRT sehr gute Therapietoleranz / wenig G3 Spät-Effekte (Nekrose)
3. sehr hohe Lokalkontrollraten (>85 - ~95%)
4. falls WBRT: HA so möglich

vielen Dank für
Ihr Interesse